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Determinants of PRO-industry interactions in pharmaceutical R&D: the case of Mexico

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Abstract

Interactive learning, particularly between firms and public research organizations (PRO), nurtures the dynamics of systems of innovation. Limited interaction contributes to explain poor performance in R&D and ultimately, in innovation by developing countries. But why this is so? Based on evidence from the pharmaceutical industry in Mexico, this paper identifies some determinants of PRO-industry interaction for pharmaceutical R&D. Particular attention is granted to factors hindering such interactions; arguably the barriers differ throughout the diverse stages of the R&D process. The paper decomposes the Research and Development processes, thus it is possible to identify determinants to interactions in each of those instances. Drug development is further split in two stages: clinical research and drug manufacturing. The analysis indicates that macroeconomic and business environments, firms' strategies, ethical considerations, incentives and perceptions of PRO-industry interaction among the agents in the system, support/hinder interactivity in pharmaceutical R&D.

Keywords: Public research organization-industry interactions; pharmaceuticals R&D, Mexico
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1. Introduction

Learning and innovation are predominantly interactive, socially embedded processes that take place within particular socioeconomic, institutional and cultural contexts (Freeman 1995; Lundvall et al 2002). Innovation is a complex process that involves strategic choices, concurrent (inter) actions and knowledge flows among agents within systems of innovation. Agents are heterogeneous, from firms to knowledge producer and research organizations, intermediary actors, regulatory and policy making bodies, and institutions -as laws, rules, norms, and routines (Edquist 2004). Distinct agents face and respond differently to diverse incentives and obstacles to innovation.

Notwithstanding the heterogeneous ecology characteristic of systems of innovation, the literature recognises firms as being responsible for most innovations (Nelson and Winter 1982). And yet the systemic nature of learning and innovation implies that no matter how competent individual firms are in a given area, such competences are bounded; abilities to carry out search processes are limited (Cohen and Levinthal 1989 and 1990). Firms face problems in performing innovations which require knowledge outside their immediate area of expertise; firms must be able to interact with and gain access to diverse knowledge sources (Arora et al 2001; Cohen, et al., 2002).

Research strides to understand the determinants, benefits and policy interventions supporting interactivity within systems of innovation. Interactions between universities and research centres, hereafter public research organizations (PRO), and firms play prominent roles in the literature (Freeman 1995; Mazzoleni and Nelson 2007; Eom and Lee, 2009). For instance research on national systems of innovation (NSI) and on successful catching up processes suggests that interactivity within NSI contributes to advance a country's scientific, technological and innovation capabilities, and thereby the prospects for socioeconomic development. PRO-industry interactions need to be flexible over time; they differ across knowledge fields (Monjon and Waelbroeck, 2003; Welsh et al, 2008).

PRO-industry interactions recognise that both firms and PRO produce and use knowledge. Interactivity involves knowledge flows in both directions in ways such that promote virtuous circles in knowledge production, diffusion and use. Interactions are dynamic, changing overtime as agents in the system and countries develop. The dynamics of PRO-industry interactions reflects the co-evolution of factors, such as research capabilities of PRO on the one hand, and absorptive and technological capacities within firms on the other. A firm requires complementary in-house technological efforts to absorb knowledge acquired through external collaborations (Cohen and Levinthal 1989 and 1990; Santamaría et.al, 2009).

Laursen and Salter (2004) illustrate the distinct steering power of firms, as the agent at the centre of the NSI. The authors showed that firms with "open" search strategies more likely draw from universities to underpin innovative activities. Likewise R&D intensity is a strong driver of linkages with university knowledge during innovation. As firms grow, they increase capabilities and inclination to draw from university research. The authors concluded that although structural factors bear on a firm's use of university knowledge and information, additional factors such as business strategies and managerial choices matter as well.

In this context, one of the most disquieting weaknesses of Mexico's developing NSI is that low levels of R&D accompany limited or poor interactions within such system (Cimoli 2000; Cimoli and Constantino 2000; Dutrénit et al, 2010); although some firms in the country benefit from contacts with PRO there is little fruitful interaction (Dutrénit et al, 2010). Casas (2001, 2005) indicate that firms in Mexico rely, almost exclusively, on internal learning efforts to fulfil knowledge requirements. Successful PRO-industry linkages often limit to a handful of firms in specific sectors, including metalworking, health, chemicals and pharmaceuticals. Recent policy initiatives to strengthen PRO-industry interactions, and enhanced pressures for academic organisations to identify and leverage new sources of funding have had limited success (FCCT 2006).

Whereas available research explores and maps PRO-industry interactions in developing NSI, we still know little about factors hindering such interactions. Some studies confirm that sector characteristics matter as determinants of PRO-industry interactions (Cohen, et al., 2002; Laursen and Salter, 2004; Torres et al, 2010), more research is needed approaching specific sectors in developing countries. Thus one can better appreciate why dynamic PRO-industry interactions remain limited in countries such as Mexico, or how to overcome barriers to interaction. Further research should also provide a more balanced view of the determinants and incentives to PRO-industry interactions in relevant sectors; hence it is possible to inform public policies intended to increase interactivity and thereby improved performance of developing NSI.

This paper argues that PRO-industry interactions underpinning pharmaceutical R&D in Mexico respond to several, somewhat reinforcing sources, which reflect general country conditions and industry specific factors. Determinants, and particularly barriers to interaction, differ across the distinct stages of the innovation process, notably R&D. In addressing these issues, this paper proceeds as follows: Section 2 presents the data and data sources. The analysis builds on qualitative data collected through interviews with firms, PRO and policy makers linked to the pharmaceutical industry in Mexico. Section 3 characterizes recent trends in the global pharmaceutical industry; the focus is on the prospects for developing countries. A description of the pharmaceutical innovation process is also provided. The section ends with a characterization of pharmaceuticals in Mexico. Section 4 discusses

some general trends in PRO-industry interactions in Mexico. Section 5 contains the core of the analysis; it documents determinants to PRO-industry interactions for pharmaceutical R&D in Mexico. Section 6 concludes.

2. The data

This paper builds mostly on qualitative data about pharmaceutical firms in Mexico. Primary data were collected through semi-structured interviews carried out in February-August and October-December, 2007, and a final round late in 2008. Informants included representatives of multinational affiliates and Mexican pharmaceutical firms–General directors, medical directors, R&D managers, development analysts; and the main local trade organisations: National Association of the Pharmaceutical Industry (CANIFARMA for its acronym in Spanish), the Mexican Association of the Industry for Pharmaceutical Research (AMIIF for its acronym in Spanish) and the Mexican Association of Drug Manufacturers (ANAFAM for its acronym in Spanish). Membership overlaps across these three organisations but CANIFARMA is the largest of them; its members account for 85 percent worth of the local private drug market. AMIIF conglomerates the 30 or so multinational affiliates more active in pharmaceutical research, mainly clinical trials, in Mexico.

In order to identify the actual number of pharmaceutical firms in Mexico we followed Secretaría de Salud (2005) who estimated that in 2005, 200 such firms operated in Mexico. This study approached 140 firms, mostly through CANIFARMA. In total 40 firms replied to our invitation-response rate 28.6 percent-, but only 22 provided usable data. The 18 remaining firms were unwilling to participate in the study; reasons for this included internal policies preventing them to do so, “ethical reasons” or difficulties to provide confidential information. Some firms required an official request from the local regulatory agency; reticence of individuals to provide information was due to strict confidentiality agreements signed with the company.

The interviews took an hour long on average, in the majority of cases were audio-taped and partially transcribed afterwards. For reasons of an explicit commitment to confidentiality, identity of informants and firms remains anonymous; we refer to them as Firm 01 through Firm 22; Trade1 through Trade3; and InsH1 through InsH3--see Annex 1. The interviews informed about the extent to which firms conduct pharmaceutical R&D in Mexico, activities included and reasons to do or not to do so. Emphasis was put on learning about the main opportunities/challenges derived from the general conditions for R&D in the country: research infrastructure, availability of human resources, the match between the research agendas of firms and PROs, and so on. Additional questions explored the firm’s publishing practices, the relationship with regulatory agencies and so on. Interviewees were prompted with claims by previous interviewees in order to crosscheck information.

Additional interviews took place at the Mexican regulatory agency, the Federal Commission for the Protection against Health and Sanitary Risks (COFEPRIS for its acronym in Spanish); the Coordinating Commission of the National Institutes of Health and Specialty Hospitals (CCINSHAE for its acronym in Spanish), and the Mexican Institute of Health and Social Security (IMSS for its acronym in Spanish). In all these cases the questions were similar to those posed to firms but rephrased as necessary to capture the opinion of these organisations.

Three official notes were obtained from COFEPRIS following requests through the Mexican government's portal for transparency and access to information (IFAI for its acronym in Spanish). Attendance to a specialized seminar on clinical research, LamtechInstitute (2007), informed about such activities in Mexico and Latin America as well.

Additional data stems from two surveys, conducted during 2008, on the nature of PRO-industry interactions in Mexico. The surveys took the individual as the unit of analysis. One of them targeted R&D and product development managers within firms. The working sample consists of 387 questionnaires out of a target population of 1200 firms; response rate of 32.6 percent. The participating firms split in two groups: first those who have benefited from CONACYT's research funds. A second group includes firms that have not received public funds for R&D. The control group took into account the size, sector and location characteristics of the first group of firms. Both groups include collaborative and non-collaborative firms. The distribution of firms by size, sectors and regions obtained in the received questionnaires are consistent between the two groups of firms.

An additional survey focused on researchers at PROs. An email questionnaire was sent to 10,100 researchers from the National Researchers System[1] (SNI for its name in Spanish), but the response rate was very low. We turned to a shortlist of 2,043 researchers provided by the Council for Science and Technology in Mexico (CONACYT), based on those knowledge fields that are most active in applying for public grants. We complemented this list with 1,380 researchers working in engineering departments of the main PROs in Mexico. Thus the survey included researchers independent from the SNI but that link with firms. The response rate was 14% for a working sample of 461 questionnaires. This paper discusses some general findings from such surveys; Dutrénit, et al., (2010) present more

[1] The SNI is one of the instruments supporting S&T activities with the longest tradition in Mexico. Since inception in 1984, the system promotes the formation, development and consolidation of a critical mass of researchers at the highest level, mostly within the public system of higher education and research. Member researchers receive both pecuniary (a monthly compensation) and non-pecuniary stimulus (status and recognition) based on the productivity and quality of their research.

detailed results.

Secondary sources of data included academic and industry literature and online datasets. Statistical data stem from the latest national innovation survey (Encuesta sobre Investigación y Desarrollo de Tecnología –ESIDET) carried out by CONACYT in Mexico in 2006 (CONACYT 2007). This paper used information about the pharmaceutical industry only. Secondary data sources helped to validate information obtained through interviews.

3. The pharmaceutical industry

3.1. The innovation process

Pharmaceutical innovation comprises four somewhat overlapping instances whose length and costs depend on legal, ethical, scientific and economic factors (Figure 1): (1) basic research leading to identification of new molecular targets, "New Chemical Entities (NCEs),"[2] and pre-clinical studies;[3] (2) clinical research that aims to test and eventually, certify efficacy, safety and overall socio- and techno-economic viability of mass production of new drugs or medical devices (Zivin 2000); (3) regulatory processes governing R&D, registry and commercialization of drugs; important regulatory events include: filing/obtaining patents, applications to commence clinical trials of investigational new drugs (IND), and authorization to market new drugs (NDA); and (4) manufacturing, marketing and product life-cycle support of existing drugs. In the case of new drug development this stage begins with clinical research and gears to assess economic and industrial viability of the potential new drugs. Generics drugs development, and improved drug manufacturing processes also occur at this point; a major difference is that clinical testing here seeks to prove interchangeability with the innovator drug. The model of pharmaceutical innovation in Figure 1 also applies to Mexico (personal communication, COFEPRIS, 8 January 2006).

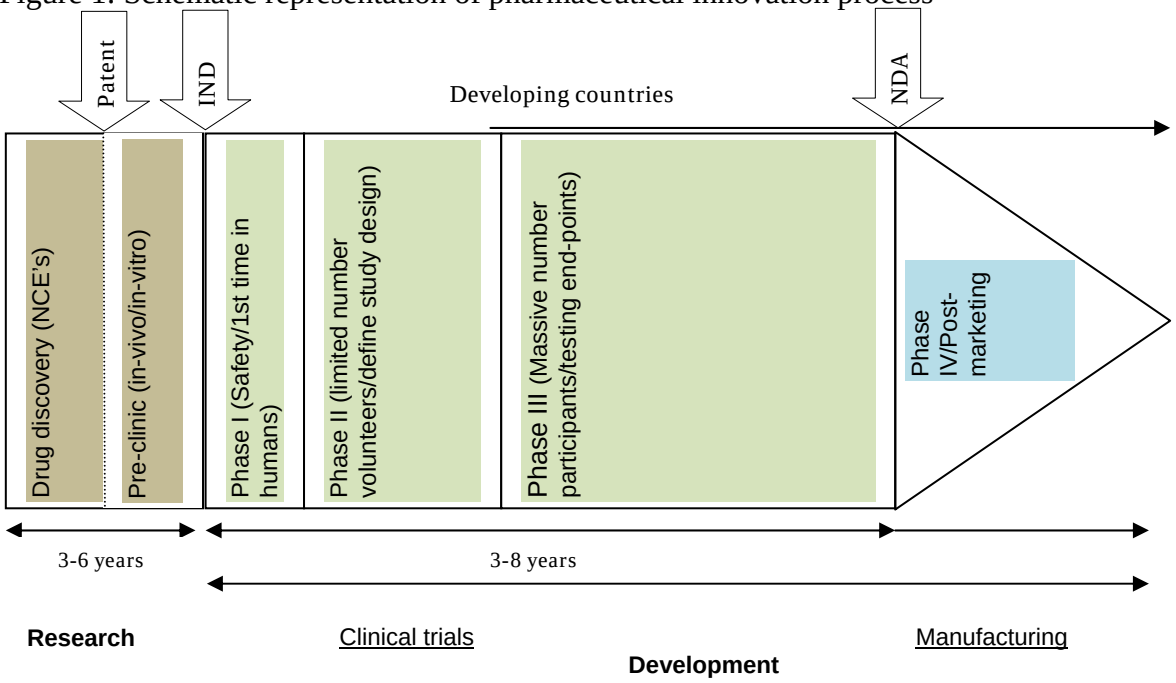
Developing countries such as Mexico contribute mostly to the advanced stages of the pharmaceutical innovation cycle as depicted in figure 1. In other words, during their contribution is during clinical trials, or in the life-cycle support of existing pharmaceutical products; the latter includes development of generics drugs. For the sake of comprehensiveness of the analysis, this paper looks at two broad dimensions of pharmaceutical innovation: Research and Development. The latter splits in two

[2] NCEs are totally new drugs, which in most cases represent significant therapeutic advances.

[3] Pre-clinical studies in animals or other models assess toxicity and other pharmacokinetic properties of prospective NCEs before tests in humans can begin. Similar tests are performed in humans during clinical research (Zivin 2000).

instances namely, clinical research and generics drug manufacturing.

Figure 1: Schematic representation of pharmaceutical innovation process



Notes: IND: Investigational New Drug; NDA: New Drug Application.
Source: Santiago (2010)

3.2. Global dynamics

The global pharmaceutical industry stands out for its socio-economic, health and ethical implications; intensive R&D efforts characterize it as a highly science-based industry. Innovation conditions strongly success in the industry, particularly at times of increased competition from generic manufacturers and a relatively slow pace of new drug innovation. Pharmaceuticals systematically rank among the top R&D expending sectors throughout the developed world (NSF 2008). Continuous exploration for technological opportunities and innovation is critical for competitiveness and success of global pharmaceutical firms. Competition in the industry is such that internal technological efforts are insufficient to respond, in a timely manner, to current market dynamics. Mergers and acquisitions, outsourcing and off-shoring, together with joint performance of R&D increasingly guide business strategies of global firms. Interactions with PROs seek to tap into external knowledge and expertise, reduce cost and speed up new drug development (Piachaud 2002; Crossley 2004; Santiago 2009).

Developing countries are expected to influence significantly future developments in the global pharmaceutical industry. By the year 2013, 17 high-growth emerging pharmaceutical markets will

contribute 48 percent of annual market growth–up from 37 percent in 2009; in aggregate terms such countries will expand by US$90 billion during 2009-13 (Gatyas and Savage 2010). China, Brazil, India, Russia and to a lesser extent Venezuela, Poland, Argentina, Turkey, Mexico, Vietnam, South Africa, Thailand, Indonesia, Romania, Egypt, Pakistan and the Ukraine are emerging economies with potential to drive the industry in the coming years. According to IMS-Health (2009) factors explaining these positive trends in developing countries include growing government expenditure in healthcare and raising demand for innovative medicines. Although the technological dynamism of firms in catching up countries generally lags behind that of large multinationals, R&D remains core for success. The major difference is that, in general, R&D in developing countries underpins incremental innovations (Cardinal and Hatfield 2000; Kim 1997).

3.3. Pharmaceuticals in Mexico

Mexico ranks among the world's largest pharmaceutical markets, and is the second in Latin America. Together with Brazil, Argentina and Venezuela, the country accounts for more than 80% of total sales in Latin America (Secretaría de Salud 2005). At the end of 2008 retail sales in the Mexican pharmaceutical market amounted to US$8.6 billion, up by two percent relative to 2007. Local infrastructure to manufacture pharmaceuticals is among the most modern in the world, often complying with US Food and Drug Administration (FDA) standards of quality and safety of products, facilities and personnel (Trade2 and firm02).

According to Guzmán (2005) and Secretaría de Salud (2005) such factors as local consumption and its ample integration to international markets give Mexico potential to become an important centre for pharmaceutical innovation. Unfortunately this potential remains largely unrealized; major bottlenecks result from an unsuitable environment to carry out R&D, gaps in health and sanitary regulations among other factors (Santiago 2010b; Secretaría de Salud 2005). Plans to effectively promote development of the industry are absent (Firms 05, 06 and 11 and Trade1). Additional gaps result from high cost of basic infrastructure and energy; tight price controls, macroeconomic risks and uncertain policy environment (Secretaría de Salud 2005).

In 2005 total innovation-related expenditure by the pharmaceutical industry in Mexico was US$132-148 million (CONACYT 2007). Investment in machinery and equipment on the one hand, and R&D on the other, are the two main components with combined shares of 80 percent of total expenditure. Nevertheless R&D represents the largest component of innovation-related expenditure, 45 percent. Investment in industrial design or prototype plants is also relevant for the industry. By contrast acquisition of software and other external technologies, and expenditure on innovation-relevant training occupy minor proportions in total investment in innovation-related activities.

Pharmaceutical innovation in Mexico characterizes by limited performance of basic research or drug discovery and growing activity in clinical research. Most technological contributions are in the manufacturing or post-marketing stage of the pharmaceutical innovation cycle, in the form of incremental innovations namely, novel analytic methods, drug delivery systems, new applications or reformulation of existing molecules, new dosage forms, vaccines and generics drugs (Trade1 and Firms 04 and 05). Firms create new excipients or recombinations of them (Firms 05 and 11, Trade1).

Pharmaceutical firms in Mexico replicate existing drug manufacturing processes in order to obtain marketing approval by local authorities (Firms 07, 11 and 13). At advanced stages of technological development firms seek to enhance quality of existing drugs. Some local firms, such as Silanes, Probiomed, Grupo Techsphere and Alpharma, have attained or are developing capacity to research NCEs based mostly on biotechnology techniques and closer interaction with public and private research organisations in Mexico and abroad. Biotechnology is a viable though still expensive way to build in-house R&D capabilities (Firms 03, 06 and 10).

According to CONACYT (2007), in 2004 and 2005, 59.1 percent of pharmaceutical firms in Mexico performed in house R&D, the majority of which, 94.8 percent, obtained some kind of result (Table 1). By far product innovations are the most frequent. Firms that perform R&D with some kind of results (181) introduced, on average, 16.8 new or improved pharmaceutical products. The number of firms introducing some new or improved process is considerably smaller (75); on average firms introduced some 15.7 process innovations.

In Mexico most pharmaceutical innovations are new to the country or new to the firm. In general firms tap into available knowledge to adapt products and/or processes to the local market. Few firms have produced drugs which are completely new to the world (Firms 04, 10, 11 and 14); these are mostly recombination of existing drugs. Sales revenue makes little distinction between new and improved products; new products represent 53.0 percent of total sales. The figure contrasts significantly with the sales of innovative products by the whole of the manufacturing sector, up to two thirds of total sales. Although pharmaceuticals record a larger R&D intensity in terms of sales, sales revenue from new or improved products is lower than manufacturing as a whole.

The larger number of pharmaceutical patents taken in Mexico is by multinationals; this supports marketing of innovative drugs, particularly to serve the private market. By contrast low patenting activity of local agents reflects the limited learning activities carried out in the country. According to Guzmán (2005) the bulk of pharmaceutical patents taken by Mexican agents correspond to individuals

or research organisations; only a minor share are taken by domestic firms and traduced into marketable products.

Table 1. Innovative performance of the Mexican pharmaceutical industry, 2004-2005

	Pharmaceuticals	Manufacturing
Total firms	323	16398
Carried out R&D[1/]		
Yes	191	4,090
With results	181	4,040
No	132	12,307
Results from R&D		
Products	3,043	35,471
Yes[1/]	181	3,891
% of total firms	56.3	23.7
Processes	1,178	9,444
Yes[1/]	75	2,001
% of total firms	23.2	12.2
Innovations by degree of novelty (per cent)		
Firm	Country	World
21.4	77.6	1.0

	Pharmaceuticals	Manufacturing
Distribution of sales by novelty of product (%)		
New	24.2	31.8
Improved	28.8	36.4
No change	47.0	31.8
Total	100	100
Patents		
	Applied	Granted
Mexico	64	22
Abroad	56	11
Total	119	33
Linkage activity in pharmaceuticals[1/]		
	Product/Services	Process
In house	138	69
Research Centres	10	4
Universities	15	0
Other firm	18	2
Total	181	75

Notes: [1/] Number of firms
Source: Santiago (2010) with information from CONACYT (2007)

4. PRO-industry interactions in Mexico

4.1. National context

Interactivity within the Mexican NSI is limited. CONACYT (2007) documents that in 2005 only two percent of innovation projects carried out by firms involved PRO-collaboration. In that same year the share of university R&D financed by the industry was equivalent to one percent of total R&D by Mexican universities; the figure contrasts significantly with the OECD's average of 6.1 percent.

Notwithstanding the limited interactivity in the Mexican NSI, the two surveys on PRO-industry linkages described in Section 2 revealed that such interactions are stronger than usually expected; firms link with universities for consultancy services but also for some joint R&D. Nevertheless suppliers and competitors persist as being the main information/knowledge sources for firms. These findings mirror those of Cohen, et al., (2002), Laursen and Salter (2004), Eom and Lee (2009). Formal and informal modes of interaction are multiple and complementary; however human resources hiring and training, and research-based collaborations are the most important.

As expected by the knowledge-based theory of the firm PRO-industry interactions sustain activities either that increase a firm's technological capabilities, or that complement such capabilities (Grant 1996). The importance of PRO-industry interactions augments with the complexity in the expected innovation, the more novel the innovation the more dynamic the PRO-industry linkages. Human resources mobility facilitates knowledge flows between firms and PRO. Geographic proximity plays also important role as determinant of collaboration.

4.2. PRO-industry interactions in pharmaceuticals

Table 1 shows that in Mexico three quarters of firms that introduced some product innovations did so without interacting with other agents. The disconnection is more evident in the case of linkages underpinning process innovations, only a minor share of innovative projects involved cooperation. In fact linkages with universities were of little or no relevance at all for process innovations. CONACYT has undertaken some corrective actions to promote interactivity in the Mexican NSI, namely: adoption of fiscal incentives to R&D, and creation of sectoral and regional research funds. CONACYT funds projects jointly performed by firms and other organisations. In 2006 investment in such projects added up to MX$3,999.8 million (US$366.9 million) (Table 2); 481 firms participated in 1,616 projects. The two latter figures more than tripled compared to 2001. Notwithstanding these efforts, interactivity remains modest (FCCT 2006).

Table 2. CONACYT's investment in projects involving interactions of firms and other agents, 2001-2006

	2001	2002	2003	2004	2005	2006
Pharmaceutical industry						
Firms[1/]	9	16	27	35	50	48
Projects[1/]	31	95	132	202	278	273
Investment[2/]	3.1	3.2	5.7	11.6	17.9	29.0
Inv/project[3/]	100.8	33.2	43.1	57.2	64.3	106.1
Share in total						
Firms[1/]	6.3	7.4	11.4	9.8	8.2	10.0
Projects[1/]	6.1	11.5	15.1	15.4	13.3	16.9
Investment[2/]	6.5	5.0	10.1	9.5	6.2	7.9
Total						
Firms[1/]	142	216	236	357	608	481
Projects[1/]	506	824	873	1308	2083	1616
Inv/project[3/]	95.2	76.1	64.8	93.0	137.4	227.1

Notes: [1/] Number; [2/]US$ million, 2006=100; [3/]US$ Thousand
Source: Author with information from CONACYT

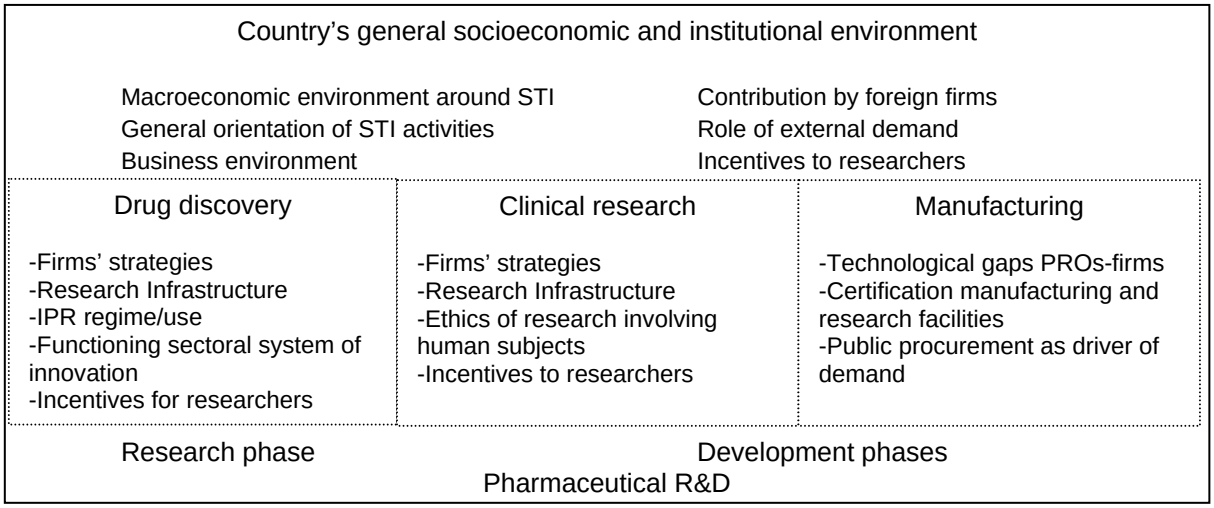
Participation of pharmaceutical firms in CONACYT-sponsored R&D funds increased considerably between 2001 and 2006, from nine to 48 firms. This notwithstanding, the figures suggest inconsistency in resource allocation. The average allocation per project was constant between 2002

and 2006. More detailed information about the number of applicants and corresponding funding requirements is missing; hence it is difficult to see how the base of firms with capacity to apply for public grants is changing over time. Although the number of both pharmaceutical firms and projects has increased, investment per project has hardly followed pace. The number of pharmaceutical firms supported by CONACYT is a minor fraction, about ten percent, of those that could potentially participate. We now explore some factors likely to explain the low interactivity in pharmaceutical R&D in Mexico.

5. Determinants to PRO-industry interaction in pharmaceutical R&D in Mexico

In Mexico low PRO-industry interactions reflect several reinforcing factors along a continuum. At a macro level the structure and functioning of the NSI is poorly conducive to such dynamic interactions, it characterizes by low investment in R&D, inadequate or limited research infrastructure. At a more disaggregated level, firms and PRO respond to different, somewhat difficult to conciliate incentives and aspirations; scientific communities face limited, even contradictory incentives to interact with firms. Figure 2 illustrates how determinants to interaction differ across different stages of the pharmaceutical R&D process.

Figure 2. Determinants of interaction in pharmaceutical R&D in Mexico.



Source: Santiago (2010)

5.1. General country conditions

The *macroeconomic environment around STI* in Mexico is poorly conducive to dynamic PRO-industry interactions. Mexico endures bottlenecks in such areas as STI policy-making and

implementation, low incentives to R&D as the basis for successful business strategies, little interaction between relevant components of sectoral and NSIs, scarcity of human resources and inadequate research infrastructure (FCCT 2006). For more than a decade R&D expenditure has stagnated at around 0.40-0.46 per cent of GDP, somewhat below the 0.88 per cent recorded by Brazil, the largest economy and pharmaceutical market in Latin America (CONACYT 2007). Public investment in STI is also equivalent to only 0.36 per cent of GDP.

Notwithstanding all the above the prospects for health research are somewhat better than those of other activities; over the last eight years or so public expenditure in health-research grew at an average rate of 13.7 percent. Unfortunately stagnant total public expenditure results in trade-offs between expanding investment in health and reduced support to other sectors.[4] The good news is the growing private expenditure in R&D. In 1997-2005 private investment increased at a pace of 19.0 percent per annum; from a share of 16.9 percent in 1997, it reached 41.5 percent of total expenditure in R&D in 2005 (CONACYT 2007).

The *business environment* in Mexico induces poor incentives to R&D in general, and for PRO-industry interactions in particular (Secretaría de Salud 2005). FCCC (2006) reports the dearth of domestic demand for products with more substantial domestic technological content; local firms privilege import of technologies developed elsewhere. In the case of the pharmaceutical industry, firms frequently decry the aggressive liberalisation and deregulation of the sector without accompanying policies to support development of the industry; firms face predatory behaviours from the public sector resulting from price controls, inconsistent application of IPR laws or public procurement mechanisms that privilege price over quality (Firms 02, 03, 04, 05, 06, 10 and 11). Related to this is the concentration of sales by domestic firms in the low price, high volume public sector; sales revenue hardly sustain enhanced in-house technological efforts (Firms 01, 03, 06 and 11).

External demand as driver of local technological efforts remains insufficiently exploited. Hikino and Amsdem (1994) and Kim (1997) documented the key role played by export oriented business strategies for the successful catching up of some dynamic firms in South East Asia. Kim et al, (1989) noted similar experiences in pharmaceutical firms. In Mexico exports, particularly to the large US market, remain insufficiently exploited to strategically support technological progress by local pharmaceutical firms (Firms 03, 06, 12 and 14). To a large extent such passive behaviour reflects high

[4] See FCCT (2006) and Dutrénit et.al., (2010) for a more ample discussion about the characteristics of expenditure in S&T in Mexico.

cost to obtain marketing licenses in the US,[5] insufficient manufacturing capacity and limited R&D (Trade1). The limited export orientation of Mexican pharmaceuticals contrasts significantly with that of some of the larger Indian firms: "...the US market is such that you have to continuously keep launching the products to be able to compete and to retain your place in the market. You cannot launch four products and then sleep for the next one year, you have to continuously launch 10, 15 new products in a year. It requires a whole lot of commitment of resources, but also the company has to be geared towards servicing the market. And the Mexican companies so far, you know, they are pretty comfortable in Mexico; and to be able to service the more dynamic US generic market, I don't think they have the mindset yet" (Firm12).

Foreign firms induce limited incentives for domestic R&D: Mexico hosts affiliates of large multinationals from countries with long tradition in pharmaceutical innovation, namely the US, Germany, Switzerland and France; the country increasingly attracts affiliates from such new players as Spain and India as well. Multinational operations range from purely commercial to large-scale manufacturing and some R&D with distinct degrees of sophistication. Multinationals respond for the highest levels of modernisation and automation of the local industry. By contrast drug discovery is exceptional to nil; R&D concentrates in formulation, new applications or niche products tailored to the local market (Firms 01, 03, 07, 13, 17, 18, 20 and 21). Multinationals increasingly perform clinical research partnering with local research organisations, mainly public hospitals (Firms 03, 07, 13, 17, 18, 20 and 21; Trade2; InsH1 and InsH3). Santiago (2009) indicates that relocation of clinical research reflects strategies intended to exploit country specific characteristics such as population size, epidemiological profiles and high prevalence of diseases affecting both developed and developing countries. Unfortunately relocation of R&D into developing countries seldom translates into enhanced dynamism by local innovative activities.

Researchers and businessmen have distinct understanding of PRO-industry interactions. In the pharmaceutical industry PRO-industry interactions respond to two types of factors: On the one hand there is insufficient awareness and mutual understanding of the activities performed by both firms or PRO researchers, and the benefits of potential partnerships (Firms 05 and 06; Dutrenit et al, 2010). Arza and Vazquez (2008) report similar findings in Argentina. On the other hand there is uncertainty on the extent to which PRO-industry linkages increase the likelihood of succeeding in innovation. Eom and Lee (2008) assert that a large part of the knowledge from universities is intangible with uncertain impact on success in innovation.

[5] Licenses to manufacture drug in the US are costly, costs vary depending on whether the product is innovator or generic; in other cases bails and insurances on compliance can be involved (Secretaría de Salud. 2005). Rights to manufacture serve effectively as entry barriers.

Firms and PRO look at STI through different eyes; both agents face different incentives and motivations, *publish or perish* clashes with *time to market* incentives and rewards (Firms 05, 06 and 11). This is the classic dichotomy widely documented in the literature (Pavitt 1998; Stephan 1996; Stephan and Audrestsch 2000). In Mexico debate exists about the adequacy of incentives for researchers to work towards applied research, to take patents or develop new products in connection with firms (AMC-FCCT 2005); researches frequently ignore potential benefits of doing so (Firm 05 and Trade2). Researchers benefiting from public programmes such as the SNI, primarily seek publication in international scientific journals and citations as core curricular activities (AMC-FCCT 2005). Some recent measures in the fields of health sciences grant increased importance to technological developments-patents, prototypes, specialised software, technical reports, industrial secrets, copyrights, and so on, as valid products supporting promotion within the SNI (Secretaría de Salud, 2005).

The perception of value of PRO-industry interactions differs across the research community; this complicates PRO-industry linkages. Researchers whose work orient to applied research or technology development, tend to interact more with firms, although interactions in basic science are not negligible (Dutrénit, et al., 2010). Whereas firms perceive universities mostly as sources of qualified human resources, the main role of public research centres is that of using R&D to solve concrete problems. By contrast PRO researchers see themselves as important knowledge generators for firms. Casas (2001 and 2005) indicate that firms in Mexico believe that they possess enough R&D capacities; hence they are not particularly pressed to seek external knowledge. In the spirit of Cohen and Levinthal (1989 and 1990) limited absorptive capacities complicate the identification and use of external knowledge.

5.2. Determinants of PRO-industry interaction across stages of the R&D process

This paper argues that the nature and to a certain extent, the importance of determinants of PRO-industry interactions vary along the different stages of the innovation cycle of an industry. Such different stages involve distinct kinds of agents, activities and knowledge flows; they require diversified skills, professional backgrounds, performance indicators and so on (Henderson and Cockburn 1994; Omta et.al, 1997). In the case of pharmaceutical innovation, different managerial approaches support drug discovery on the one hand, and drug development on the other (Chiesa 1996). Research characterizes by unpredictable timing, informality in the structure of work, modes of expenditure and uncertain results. By contrast Development features more predictable timing to conclude tasks, formality in the organisation and conduction of activities, considerably larger expenditure and planned results (Chiesa 1996). Whereas key in research is “creativity”, key in

development is “organisation”; furthermore research and development split in both organisational and physical terms (Chiesa 1996). While firms conduct clinical research in connection with PROs, drug development, particularly generics, occurs mostly in-house with little reliance on PROs.

The following paragraphs explore how determinants of PRO-industry interactions differ across the several stages of the pharmaceutical R&D process described in figure 1; the focus here is on a developing country such as Mexico. The analysis distinguishes between (1) basic research; (2) clinical research and (3) development of generics drugs and related process innovations. The analysis identifies factors that, according to interviews, affect with particular strength PRO-industry interactions for pharmaceutical R&D.

5.2.1. Basic research

Mexico possesses facilities to perform new drug-related research; yet activity in that area is incipient. Basic research takes place mostly at PRO with limited links to the industry. Why firms do not capitalise on those activities?

Mexico integrates as manufacturing centre within the global strategy of pharmaceutical firms. In line with literature on internationalization of R&D (von Zedtwitz and Gassmann 2002), and from a business strategy view point, multinationals look at Mexico as a manufacturing location and consumption market more than as an R&D centre. Mexico lacks technical infrastructure, adequate regulatory frameworks around health-research and a critical mass of human resources sufficiently experienced in drug-related R&D (Firms 01, 02, 06, 13, Trade1, InsH1). A few public research centres meet world-class standards and possess adequate research methodologies and procedures, but this is insufficient to attract larger investments in R&D (Firms 01, 05 and 06). PRO lack sufficient equipment (i.e. column chromatography), in both the numbers and degree of sophistication required to, often simultaneously, carry out the massive amount of biological and chemical testings underpinning new drug discovery.

The director of research at Firm 13 pointed out: “[The] Tests [we carry out] often should run simultaneously and at considerable precision and speed. [Mexican researchers have little or no experience in] conducting lead discovery projects, in understanding the physicochemical structure of the processes under research; for instance, to test for systemic or crossed effects of lead targets, particularly when processes of hypothesis testing involve combinations or simultaneous analysis of different molecules or substances”. Whereas R&D in a majority of Mexican firms strides to ensure interchangeability of generics products, multinationals are “exploring, testing and solving new hypotheses” (Firm 13). The regulatory environment complicates the obtaining of permissions to

transport, sometimes hazardous materials and samples for subsequent testing in new drug related research (Firms 13 and Trade2).

According to Zúñiga and Combe (2002) it is difficult to expect significant increases in R&D expenditure by multinational pharmaceuticals in developing countries. Notwithstanding patent reforms, multinationals maintain their traditional concentration of corporate R&D laboratories in their parent countries. Additional, complementary factors are needed to attract research facilities into Mexico, including: (i) more coherent STI policies; (ii) better linking public research to specific health challenges and epidemic profiles of the Mexican population; (iii) direct promotion of pharmaceutical R&D; and (iv) raising quality standards of PROs' infrastructure and staff.

Inadequate processes and regulations for the definition and handling of intellectual property rights (IPR's) at PRO hinders access to research with potential pharmaceutical use. It is problematic to negotiate technology transfer or joint development projects when no one owns the technology (Firms 04, 06 and 13, trade1 and Trade2). Equally problematic is to value potential technologies; both researchers and businessmen find difficult to agree on faire prizes and distribution of eventual benefits stemming from new pharmaceutical products (Firms 05 and 06). According to firms, scientists think their work has potential to turn into something of great value and ask sizable compensations in return for whatever knowledge they share with firms (Firms 03 and 05). The opposite works too, with researchers' complaints about the low value firms tend to grant to potential profitable scientific discoveries (InsH3).[6]

The sectoral system of innovation underpinning pharmaceutical R&D is fragmented. Limited interactivity for pharmaceutical R&D in Mexico occurs between firms and research organizations, but also among PRO researchers and between these and other government institutions. For instance, the leader of the R&D department at Firm 13 commented that "Although diabetes is one of the most prevalent diseases in Mexico, so far there are no specific mechanisms whereby public health and S&T organisms, healthcare institutions, research organisations and firms can join forces to develop new drugs or other products for such population. Everybody is working on his/her own agenda without proper assessment of how research results may be applied and translated into new products". Firms 03, 05 and 06 supported this argument by noting the little interaction among firms in the industry in order to innovate. Firms find real difficulties to identify suitable partners and to build proper niches to

[6] In this line Dutrénit, De Fuentes and Torres (2010) found that interactions through patents negatively affect intellectual benefits that Mexican researchers perceive from this form of interaction. Efforts to link through patents seem to greatly exceed the benefits obtained from them.

develop proprietary technologies; clearly a symptom of low in-house technological capacities (Cohen and Levinthal 1989 and 1990).

Firms and PRO researchers have distinct strategic orientations. Pharmaceutical firms sponsor relatively little research projects at PRO. An additional point of contact is via awards and recognitions, through organisations such as CANIFARMA, to interesting basic research projects in the areas of health, medicine and pharmacology. In general however such projects seldom make it to the development stage; researchers are not interested in pursuing further development, applications are not immediately obvious or linkages with the industry fail to prosper (Firms 05, 11 and Trade1). According to Trade1 between 2000 and 2006 some 160 projects registered to the CANIFARMA Award in health and pharmaceutical-related research, with around eight projects obtaining the award. Of those successful projects no more than two have eventually transformed into tangible products. Trade1 mentioned negotiations between CANIFARMA and CONACYT to design awards in support of joint PRO-industry research, together with strategies to create critical masses of projects, mobilize resources and complementary assets from distinct research organizations.

In the case of biotechnology Bolívar (1997) reported that in Mexico a major obstacle to develop industrial applications was the strong teaching or research orientation of graduate programmes in the field; they have little or no connection at all with industry needs. Firm 05 indicated that such problems persist; it stressed the "inadequate interpretation of the concept of biotechnology by Mexican policy makers. Because authorities take it as a generic sector, they tend to ignore differences in the development of applications for agriculture, food and pharmaceutical industries". The research director of Firm 3 took further this argument by stressing the mismatch in the technological specialization of firms and universities in Mexico; whereas the former focus on biopharmaceutical applications, the latter focus mostly on applications in agriculture. Such divergence reduces the scope of interaction both in training, particularly at tertiary level, and actual research (Firm 05).

Interviewees equally decried the uncertainty about whether large manufacturers of innovative products would willingly commercialise APIs developed by Mexican drug manufacturers (Secretaría de Salud 2005 and Firms 03 and 06). As noted by Hobday et. al., (2004) in the case of South Korea, catching up is problematic whenever latecomer firms fear entering into competition with their traditional input suppliers. Additional restrictions result from regulations that limit the capacity of PRO to receive funding and equipment from private organisations (Firm 6; InsH2), little linkages between public scholarship programmes and real needs for human resources in the industry (InsH1 and Firm 06), insufficient funding for R&D, and the long time and high uncertainty inherent of pharmaceutical R&D (Secretaría de Salud 2005; Trade2).

5.2.2. Clinical research

Firms' strategies, research infrastructure and the regulatory environment: The length and high cost of clinical trials compel pharmaceutical firms to seek enhanced speed, coordination, efficiency and accuracy of those activities; firms aim to reduce time-to-market, increase profits and enhance product quality. Internationalization and concurrent performance of trials in multiple locations assist such goals. Developing countries such as Mexico increasingly contribute to drug development via the off-shoring and outsourcing of clinical trials. Santiago (2009) notes that multinationals benefit from the presence of some world-class healthcare and research organisations in developing countries. Those organisations offer experience in conducting clinical research and in dealing with internationally acceptable practices governing clinical research. The later include ethics committees responsible to ensure that research protocols proceed in relatively efficient, ethical, transparent and speedy manner. Equally relevant is the nature of regulatory environments and availability of researchers with sufficient experience in the conduction of clinical research (Trade2, Insh2, Insh3 and CRO).

Mexico is an attractive site for clinical research (Santiago 2009; Firm2; Trade2), it is a leading site in Latin America. In 2005 alone research protocols spanned more than 20 therapeutic areas and involved more than 1,000 institutions and 43,000 patients (AMIIF). By linking to PRO both foreign and domestic firms avoid the need to create specialized centres, as required by Mexican authorities, to perform clinical trials. Public health and research organisations grant access to large and captive segments of population under fairly standardized research conditions; IMSS host 70-80 percent of research protocols in Mexico (InsH2 and Trade2).

Notwithstanding all the above, in Mexico the development of human resources required to further growth of clinical research lags behind the dynamics of local markets for those activities (LamtechInstitute 2007). There is also the need to improve regulatory frameworks in order to accommodate the distinct scientific content, risk profiles and other technical characteristics of clinical research, galenic developments and, in general, research involving direct testing of substances into humans (Firm05, InsH3, Trade1 and Trade2).

The role of ethics as determinant of PRO-industry interactions remains insufficiently explored in the innovation literature; this is of great relevance in the case of clinical research. A look at the operation of ethics committees in Mexico, and the relationships between researchers in the public health system and private firms illustrate this argument.

Similar to other countries, in Mexico performance of clinical research is governed, in part, by institutional review boards (IRBs) or ethics committees attached to the organisation hosting the

research protocol. IRBs are independent groups of people formally designated to approve, monitor and review biomedical and behavioural research involving humans; the aim is to protect the rights and welfare of voluntary study subjects. In Mexico notable barriers to PRO-industry interactions result from deficient conformation of IRB's, excessive bureaucratic procedures, lack of coordination and duplication of responsibilities, even contradictory decision-making within public hospitals. For example Trade1, Firm01 and InsH2 decried contradictory resolutions in approval and funding mechanisms between the central research management at IMSS, and the IRBs at local hospitals of the same institute.[7] Poor coordination delays regulatory approval of research protocols and increases uncertainty and overall transaction costs for the firm (Trade1 and Trade2).

Ethics influences trust and thereby a researcher's perception about the adequacy of linking with pharmaceutical firms; concerns are strong as "unethical" behaviours in the industry do happen (Santiago 2010b). Blumenthal (2004:1886) identify some such behaviours involving physicians and drug companies from "the seemingly trivial (e.g. the ubiquitous dispensing of gifts, such as pens and pads with drug names inscribed) to the much more troubling (e.g. the ghost-writing of articles for academic physicians, the payment of large honoraria and consulting fees to prominent physicians who extol the virtues of company products, and the support of lavish trips and entertainment for physicians who commonly prescribe company products)." Firm 05, InsH1, InsH2 and InsH3 coincided that some of the aforementioned practices occur in Mexico; suspicion and controversy around PRO-industry relationships hinder collaboration, or at least, the likelihood to openly report interactions (InsH1 and InsH2). Greater concerns refer to medical doctors that conduct clinical research outside the public research and health systems, respectively. Observance to self-imposed industry ethical codes of conduct is also problematic (Gómez, 2009).

Is clinical research intellectually challenging and rewarding? Additional constrains for Mexican researchers to link with pharmaceutical firms result from the perception that such interactions are insufficiently challenging from an intellectual viewpoint. Multinationals reserve the design of clinical research protocols to staff at the parent location (Firms 01 and 07). Researchers in public hospitals and related organisations in Mexico can feel exploited (InsH2 and firm 05); or merely required to follow directions from sponsoring companies (CRO and InsH2). This reduces incentives to collaborate as participation in clinical trials is like doing "maquila"[8] of research (InsH1).

[7] IMSS is the main locus for new-drug related clinical trials in Mexico.

[8] The term "maquila" is borrowed from manufacturing activities denoting purely assembly, low value added, routinely activities performed by line-workers.

Global pharmaceutical firms approach product development assuming that drugs would be marketed in different locations throughout the world. Accordingly research protocols usually consider the specific physical and socio-economic conditions of all those different regions (Firms 01 and 13). Such vision is seldom shared by researchers who are not customarily exposed to the requirements of distinct regional markets for pharmaceutical products (Firms 9, 10, 11, 13 and Trade1).

5.2.3. Drug manufacturing and development of generic drugs

Pharmaceutical firms can be characterized according to the type of intellectual property rights they rely on. “Innovator companies” specialize in the development and manufacturing of innovative products protected by patents, while generic manufacturers produce drugs whose patent has already expired. Finally there are firms that participate in both markets (Santiago 2010). Pharmaceuticals in Mexico specialize in the manufacturing of generic drugs. Accordingly the subsequent analysis focuses on factors determining PRO-industry interaction in relation to generics drugs development and innovations in drug manufacturing processes.

In Mexico, development of generics drugs starts three to four years before patent expiry of the innovator product; the goal is to reproduce the knowledge behind the innovative drug while ensuring bioequivalence and bioavailability of the generic drug. In most cases, the choice of products considers current product portfolios; what firms already know. Nevertheless expected benefits increase if firms can enhance the characteristics of the innovator drug; this includes relatively simple improvements in product packaging, reformulation or recombination of existing molecules. By contrast, new products include new applications of existing drugs, often in different therapeutic areas. The search for new knowledge often relates more to the methods and techniques to synthesize the components---biotechnology---than to the characteristics of the drug itself (Kale and Little 2007).

PRO and firms face distinct levels of technological attainment. Table 1 revealed the limited PRO-industry interaction for process innovations in the pharmaceutical industry. This reflects the disconnection between the scientific and technological capabilities of firms and PRO in Mexico. Firms focus on the development of generics drugs, while PRO seek to advancing the technological frontier (Firms 03, 06 and 11). Firms rely strongly on in-house knowledge sources, or on external suppliers, particularly APIs, to find technological solutions (Firms 05 and 06). By contrast PRO researchers perceive as insufficiently challenging to work on projects that do not result in publications or outstanding scientific findings (Firms 03 and 05; InsH1, InsH3). Selective reporting of research results according to commercial interests vitiates incentives for PRO-industry interactions (InsH1).

Pharmaceutical firms need to ensure that drug manufacturing processes meet strict standards of quality and safety for human consumption; in practice this leads to adoption of internationally accepted Good Manufacturing Practices.[9] According to businessmen, Mexican researchers often fail to fully appreciate these several legal procedures required to test, develop, escalate, manufacture and market (new) drugs (Firm 05 and Trade2). Development of potential new drugs requires time, considerable financial resources, advanced and properly certified facilities including laboratories, pilot plants and personnel; these are not always available at Mexican PRO (Firms 04, 05, 06, 12 and 13 and Trade2). Strategies to overcome the aforementioned limitations are diverse. Firms 04 and 06 reported to have invested in laboratory equipment and manufacturing infrastructure inside PRO. Whereas the former firm gained access to basic research facilities and interaction with PRO staff, the latter developed an exclusive API supplier. These strategies promote knowledge transfer, and help PROs to learn about the best laboratory and manufacturing practices required by the industry.

Casas (2001) indicated that training is one of the main reasons for PRO-industry interactions in Mexico; however PRO often fail to meet industry's requirements. Both Mexican and multinational firms decried the lack of adequate infrastructure at universities: "it is hard to replicate and learn about the most modern synthesis and analytical techniques, manufacturing and laboratory practices used by the industry" (Firm 03). Lack of "faculty with sufficient experience and understanding of the industry" (Firm 03), (exacerbates) difficulties to observe confidentiality requirements of firms (Firms 03 and 06). Learning through interactions with input suppliers tend to be more important for the firm (Firms 03, 05, 06, 07).

The use of public procurement to induce demand for new pharmaceutical products with strong local content remains limited. Mexican health and industry authorities have abandoned public procurement as mechanism to promote development of the local pharmaceutical industry (Santiago 2010). Public tenders privilege prices over quality, local content, or market risks faced by suppliers (Firms 04, 05, 06 and 10); arguably this distorts the market and reduces incentives to innovate (Firm 03, 05, 06, 07, 11 and 14). The privilege on manufacturing scale and speed to market over quality effectively reduces the scope for PRO-industry interactions underpinning the design or improvement of products. Firms adopt survival strategies based more on the capacity to manufacture large volumes of generic products; they privilege automation and increased manufacturing capacity even if significant margins remain idle (Firm 03 and 05).

[9] GMP's cover layout and functionality of buildings, qualification and training of personnel, cleanliness and sanitation, monitoring, supervision and many other aspects, from beginning to the end, of drug manufacturing. GMP's are constantly reviewed and adjusted according to scientific and technological advances. Regulatory agencies watch closely this requirement even by conducting physical inspections of productive facilities.

6. Discussion and concluding remarks

Innovation scholars emphasize the key role of PRO-industry interactions for good performance of systems of innovation; interactivity brings together complementary assets, facilitates knowledge sharing, problem solving and the co-evolution of technological capabilities. Researchers devote significant efforts to understand determinants of PRO-industry interactions and their effects on the functioning of systems of innovation. Alternatively, the interest is in identifying the main actors and channels underpinning interactivity. This paper both contributes and extends this body of literature.

This paper looked at determinants of PRO-industry interactions in Mexico who, similar to other developing countries, characterizes by limited interactivity and consequently, poor innovation performance. The paper asked what limits interactivity in developing system of innovation. Empirical evidence refers to the pharmaceutical industry in Mexico. The paper explored the socioeconomic context in which pharmaceutical firms operate, how the country contributes to pharmaceutical innovation, and the role PRO-industry interactions play in each stage of the pharmaceutical R&D process. Interactivity is of strategic importance, it helps firms to keep abreast of developments in (new) drug-related R&D. In Mexico this is not always possible as diverse components of the system of innovation remain fragmented, insufficiently connected or, in fact, non-existent.

A key contribution to the literature resulted from the decomposition of the pharmaceutical innovation process; hence the analysis identified the different instances of the process, notably R&D. By proposing this type of approach the paper expands traditional studies centred on exploring where, when and how firms and PRO interact. It illustrates the pertinence to look beyond national and cross-sector perspectives that fail to take fully into account the nature of innovation in specific industries. Arguably, such distinction influences the characteristics of PRO-industry.

Decomposition of the pharmaceutical R&D process mirrored previous studies by Crossely (2004), Gassmann and von Zedtwitz (1999) and Chiesa (1996). The approach illustrated the complexity of the R&D process, identified the agents involved across those different stages and consequently, the diverse factors that either promote or hinder interactivity for pharmaceutical R&D.

The paper showed that PRO-industry interactions depend on factors pertaining to the macroeconomic environment, the availability and quality of research infrastructure and human resources, and the structure of IPR regimes. Moreover the paper showed that the way in which all those factors interplay differs throughout the distinct stages of pharmaceutical R&D. Accordingly, strategies to improve research infrastructure and human resources, for instance, need to carefully consider the

characteristics of both the processes and the people involved in basic research-drug discovery-, as opposed to those contributing to clinical research–hypotheses testing-, or drug manufacturing-scaling of new drugs, chemical synthesis of existing drugs, or development of generics drugs.

The paper substantiated the importance of the institutional environment as determinant of PRO-industry interactions. IPR regimes, regulatory mechanism and notably, ethics of research involving humans influence differently PRO-industry interactions. Additional factors relate to the motivations, aspirations and mechanisms to evaluate, sanction and reward people involved in PRO-industry interactions. The structure of incentives accommodates both “short-sighted” businessmen and “ivory tower” academics as factors shaping PRO-industry interactions. Enhanced linkages require translators, facilitators that bring together scientific work and commercial interests. Adequate observance and enforcement of IPRs should accompany codes of practices respectful of the ethos of academic work. Both academics and businessmen need to be more open, willing to learn from and understand each other.

In the aggregate a series of indirect and direct factors shape the scope and space for PRO-industry interactions underpinning pharmaceutical R&D. The macroeconomic environment around R&D, innovation more broadly defined, creates or suppresses the conditions for more active innovative behaviours of both PRO and domestic firms. The latter can miss opportunities to learn and innovate by taping into foreign direct investment and participation in export markets; business strategies geared mostly to survival narrow the space for sustained and more systematic in-house technological efforts.

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Annex 1. General description of interviews carried out as part of this study

Firm	Origin	Employment	Sales[1/]	Years[/2]	interview	Contact	Duration[/3]
01	Foreign	210	360000	<3	25/Jun/07	Director general	63
02	Foreign	1100	3119745	>50	11/Jul/07	Plant manager	
					20/Mar/07	Supervisor Manufacturing	75
					26/Mar/07	Staff Manufacturing	60
03	Mexican	n.a.	281775	>50	17/Jul/07	Plant manager	104
					17/Jul/07	Development manager	81
					17/Jul/07	Research director	88
04	Mexican	421	n.a.	~30	02/Jul/07	CEO	31
05	Mexican	343	450000	~40	11/Jun/07	CEO	92
					19/Jun/07	Plant manager	109
06	Mexican	n.a.	416394	~40	07/May/07	Director General Development manager	110
					04/Jul/07	Development manager & two staff members	
07	Foreign	808	2228675	~40	02/Apr/07	Director General	34
					10/Apr/07	Communications manager	55
					16/Apr/07	Medical and regulatory affairs manager	32
08	Foreign	1100	n.a.	>50	16/Feb/07	Latin America, Human resource management affairs	120
					13/Mar/07		90
					16/Mar/07	Technical operations	75
09	Mexican	n.a.	n.a.	>50	09/Mar/07	Former CEO assistant	60
10	Mexican	n.a.	n.a.	>50	07/Dec/07	Former Director General	76
					16/Jul/07	Head R&D department	89
11	Mexican	770	600000	+30	27/Jul/06 27/Feb/07	Operations director	120 75
12	Foreign	n.a.	n.a.	<4	11/Jul/07	Director General	19
13	Foreign	>1000	n.a.	>50	30/Jul/07	R&D director	47
					30/Apr/07	Development manager	31
14	Mexican	>1000	n.a.	>50	23/Nov/07	R&D director	71
15	Foreign	>1000	4583905	>40	26/Jul/06	Human resource technician	60
16[4/]	Mexican	>30	n.a.	>20	19/10/07	Director general	---
17[4/]	Foreign	>1000	n.a.	>30	14/Aug/07	Medical director	---
18[4/]	Foreign	>1000	n.a.	>50	19/Aug/07	Communication director	---
19[4/]	Mexican	>30	11000	>70	14/Aug/07	Director general	---
20[4/]	Foreign	90	n.a.	3	14/Aug/07	Operations director	---
21[4/]	Foreign	>350	n.a.	>70	14/Aug/07	Medical director	---
22[4/]	Mexican	>40	n.a.	4	14/Nov/07	Director general	---
Trade1	---	---	---	---	26/Mar/07	Director research	100
Trade2	---	---	---	---	03/May/07	Director communications	52
InsH1	---	---	---	---	12/Jul/07	Coordination	23
InsH2	---	---	---	---	09/Oct/08	Research coordination	90
InsH3	---	---	---	---	18/Apr/07	Director	35
CRO	---	---	---	---	04/Apr/07	Clinical research monitor	60

Notes: 1/ thousand Mexican pesos; 2/ years of operation in Mexico; 3/ in minutes; 4/ correspond to firms that returned the interview instrument together with some comments; TradeX: Trade organization; InsHX: National Health Institute; IMSS or Regulatory body; CRO: Contract research organization; n.a. Not available because the firm denied the information or provided only the share of products/markets.
Source: Author based on interviews

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